PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sex and gender differences in COVID-19: an Italian local register-based study
AUTHORS	Fortunato, Francesca; Martinelli, Domenico; Lo Caputo, Sergio; Santantonio, Teresa; Dattoli, Vitangelo; Lopalco, Pier Luigi; Prato, Rosa

VERSION 1 – REVIEW

REVIEWER	Walter, Lauren
	The University of Alabama at Birmingham
REVIEW RETURNED	17-May-2021
GENERAL COMMENTS	This is a very timely review that considers very important sex and

GENERAL COMMENTS	This is a very timely review that considers very important sex and gender variables as they relate to COVID-19 morbidity and mortality. The objective and methods are appropriate. The discussion is thorough and insightful. The limitations are accurate. One additional question I have is regarding the screening rate and practice in this region - might this have introduced a sex and gender screening bias which might need to be discussed or
	accounted for?

REVIEWER	Moretti, Anna Maria
REVIEW RETURNED	21-May-2021

GENERAL COMMENTS	The subject of this paper is appropriate for publication in the
	Journal, the scientific content is high. This is an original study. The presentation is quite clear. The methodology is well described.
	The title is suitable, the abstract clearly written, tables are necessary. The English text submitted by the Authors is quite good. This study does not require an ethical evaluation.
	Minor revisions are required.
	It is not clear how virus clearance is defined. One negative RT PCR test? Two negative tests. We suggest specifying it in the text.
	Minor english revisions are required, especially in the statistical analysis section.

What is the test used to assess the non-normality of some variables? Shapiro wilk? Kolmogorov Smirnov? Please clearly report it.

Please report in the statistical analysis section that OR were calculated in univariate chi square test analysis

It is not clear how "comorbidity" is defined in the multivariable model. Presence of at least one of the Table 1 comorbidities? We suggest specifying it in the text.

In table 1 we suggest ordering all items of last section so that the "ref" element is the first.

Conclusion: Acceptable with minor revisions.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Lauren Walter, The University of Alabama at Birmingham Comments to the Author:

This is a very timely review that considers very important sex and gender variables as they relate to COVID-19 morbidity and mortality. The objective and methods are appropriate. The discussion is thorough and insightful. The limitations are accurate. One additional question I have is regarding the screening rate and practice in this region - might this have introduced a sex and gender screening bias which might need to be discussed or accounted for?

Thank you very much for your positive feedback and the insightful observation on a possible sex screening bias. Addressing your suggestion, we have estimated the positivity rate by sex.

Reviewer: 2

Anna Maria Moretti

Comments to the Author:

The subject of this paper is appropriate for publication in the Journal, the scientific content is high. This is an original study. The presentation is quite clear. The methodology is well described. The title is suitable, the abstract clearly written, tables are necessary. The English text submitted by the Authors is quite good. This study does not require an ethical evaluation.

Thank you so much for your positive review.

Minor revisions:

Q.1 - It is not clear how virus clearance is defined. One negative RT PCR test? Two negative tests. We suggest specifying it in the text.

A.1 - Done, we have added this information.

- Q.2 Minor english revisions are required, especially in the statistical analysis section.
- A.2 The English text has been revised.
- Q.3 What is the test used to assess the non-normality of some variables? Shapiro wilk? Kolmogorov Smirnov? Please clearly report it.
- A.3 Done, thank you for the suggestion.

- Q.4 Please report in the statistical analysis section that OR were calculated in univariate chi square test analysis
- A.4 Done, we have reported this information.
- Q.5 It is not clear how "comorbidity" is defined in the multivariable model. Presence of at least one of the Table 1 comorbidities? We suggest specifying it in the text.
- A.5 Done, thank you for the good suggestion.
- Q.6 In table 1 we suggest ordering all items of last section so that the "ref" element is the first.
- A.6 Done, thank you for the suggestion.